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Original Research

The place of echinocandins in the treatment of recurrent vulvovaginal candidiasis: Case series

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Abstract

Aim: Recurrent vulvovaginal candidiasis (RVVC) is a chronic infection that affects women worldwide and affects the quality of life. We aimed to evaluate echinocandin treatment at RVVC.

Material and Methods: The patients who were diagnosed with RVVC between 2022 and 2023 were retrospectively examined. Patients who continued to experience unresolved symptoms despite prophylactic treatment and showed persistent growth of resistant Candida species in culture were selected. In total, eight patients who met the criteria were included in the study.

Results: All of the patients had previously received local and oral treatment for vaginal candidiasis. The vaginal cultures obtained azole-resistant candida species. All patients received treatment with echinocandin derivatives, and clinical and microbiological response was achieved.

Discussion: Azole resistance is frequently observed in women with RVVC. Ibrexafungerp, a new oral glucan synthase inhibitor, has received FDA approval for treatment but is not available in our country. Antifungal echinocandins showing similar fungicidal activity were used in our cases, and clinical and microbiological response was found to be high. Our findings show that echinocandins may be successful in the treatment of recurrent vaginal candidiasis.

Keywords

Vulvovaginal Candidiasis, Echinocandin, Reccurent Vulvovaginal Candidiasis

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Introduction

Recurrent vulvovaginal candidiasis (RVVC) is a common infection with a significant morbidity in women. European guidelines define RVVC as four or more symptomatic episodes of VVC over one year [1]. The global prevalence is about 4 thousand per 100,000 women [2]. The most common symptoms are vulvar itching, pain, dysuria or dyspareunia, and cheese-like vaginal discharge [3]. Microscopic examination of the vagina using light or phase contrast microscopy with saline or 10% KOH is required to confirm Candida infection. The gold standard method for diagnosis is still culture [4]. In clinical practice, the most common agent is C. albicans. However, rarely C. glabrata, C. parapsilosis, C. lusitaniae, C. tropicalis, C. krusei, C. kefyr, and C. dubliniensis can be seen as causative agents. Treatment resistance is more prevalent in non-albicans strains, presenting a challenge for clinicians [5, 6].

The first-line treatment for RVVC is induction therapy with topical antifungals or oral fluconazole followed by 150 mg oral fluconazole for six months. However, due to the high rate of resistance to fluconazole, alternative treatment regimens for RVVC are on the agenda [1].

In the treatment of RVVC, there is often azole resistance due to the long-term use of oral fluconazole and/or topical clotrimazole. In treatment-resistant VVC strains, 25-45% of the causative agents are non-albicans strains [7]. As a result, due to the variations in pathogenicity and resistance profiles against current antifungal medications, recent studies have proposed new treatment strategies for azole-resistant Candida strains [8].

Echinocandins exhibit fungicidal activity against various Candida species, including those resistant to fluconazole. Both echinocandins and ibrexafungerp seem to maintain efficacy against Candida species embedded in biofilms. Because of their fungicidal effects, echinocandins have a high therapeutic response in fluconazole-resistant albicans and non-albicans strains. Echinocandins are drugs with a high safety interval due to their low allergic potential and less toxicity to the liver and kidney compared to other antifungals. Ibrexafungerp is approved for the treatment of VVC and RVVC [9]. It is still not used in Turkey. The systemic administration of echinocandins and their ineffectiveness for oral use restrict their application in the treatment of vulvovaginal candidiasis. The approval of the new drug suggests that echinocandins, which have a similar drug mechanism, may have a role in rescue therapy. In this study, patients who received echinocandin treatment for RVVC were evaluated retrospectively.

Material and Methods

The patients who were diagnosed with RVVC between 2022 and 2023 were retrospectively screened. All patients were asked to provide informed consent. Demographic data, along with clinical and laboratory findings, treatment approaches, and outcomes, were assessed. The patient group received oral and local antifungal treatment for six months. Patients whose complaints did not resolve despite prophylaxis and resistant Candida species persisted in culture growths were selected. In total, eight patients who met the criteria were included in the study. Recurrent VVC was defined as three or more episodes of symptomatic VVC within a year by the Centre for Disease Control and Prevention [10].

Ethical Approval

This study was approved by the Ethics Committee of Toros University (Date: 2024-01-18, No: 16).

Results

The mean age was 35.2±3.4 (28-39) years. Of the patients, 87.5% were married, while 12.5% were single. All our patients had recurrent fluconazole use. Considering comorbid diseases and risk factors, one patient had IUD use (12.5%), one patient had diabetes mellitus (12.5%), and one patient had hypothyroidism (12.5%). Co-treatment was applied to only one patient. The characteristics of the patients are shown in Table 1.

The clinical samples were inoculated using conventional methods, and the isolated colonies were processed. The identification and the antifungal susceptibility profiles of the isolates have been made using VITEK 2 (bioMérieux, France), and the susceptibility findings were evaluated according to EUCAST criteria [11].

C. albicans was detected in five patients (62.5%), C. krusei (25%) was detected in two cases, and C. glabrata (12.5%) was detected in a patient. Azole resistance was detected in all cultures. Echinocandin was used as a treatment regimen of anidulafungin in four (50%) patients, micafungin in three (37.5%) patients, and caspofungin in a (12.5%) patient. All patients were treated for ten days. No growth was detected in control cultures taken at the end of treatment. The patients were considered clinically cured. No recurrence was detected in the 8-week clinical follow-up.

Discussion

There is no clear data about the incidence of recurrent vulvovaginal candidiasis in our country. As it is not a notifiable condition in most parts of the world, estimating its incidence is challenging. It is estimated that at least 75% of healthy women will experience a vulvovaginal candidiasis episode at some point in their lives [12]. The diagnosis is usually made with complaints and symptoms, and treatment is started, laboratory support is usually not needed in first-line treatment. Consequently, identifying the causative microorganisms and their sensitivity patterns in vulvovaginal candidiasis is highly challenging [12]. The rate of symptomatic vulvovaginal candidiasis in women can be considered between 17-42% [12, 13]. Obesity, impaired

Table 1. Characteristics of our patients

	Age	Species	Antibiotics	Risk factor
Patient 1	39	C.albicans	Micafungin	no comorbidities
Patient 2	39	C.albicans	Anidulafungin	Intrauterine device usage
Patient 3	37	C.glabrata	Anidulafungin	no comorbidities
Patient 4	28	C.albicans	Micafungin	no comorbidities
Patient 5	34	C.albicans	Anidulafungin	no comorbidities
Patient 6	29	C.krusei	Micafungin	no comorbidities
Patient 7	39	C.albicans	Caspofungin	no comorbidities
Patient 8	37	C.krusei	Anidulafungin	hypothyroidism + diabetes mellitus

glucose tolerance, IUD use, hormonal deficiencies, carrier status in the partner, and oral contraceptive use are accepted risk factors for RVVC [14]. Although some studies suggest that oral contraceptive use is a significant factor in vulvovaginal candidiasis, there is also evidence indicating that it does not increase Candida colonization [14].

Candidal vaginosis is typically diagnosed by isolating the causative agent through culture. Serological tests are not thought to be useful [12]. Although C. albicans is the most common agent, C. glabrata is more prevalent during the premenopausal and perimenopausal periods. In a study examining cervical and vaginal smear samples using the PCR method, C. albicans was detected at a rate of 89%, C.glabrata at 7.9%, and other Candida species at a rate of less than 2% [15].

Acute VVC can be treated locally with polyenes (such as nystatin and amphotericin B), imidazoles (including clotrimazole, miconazole nitrate, and fenticonazole nitrate), or ciclopiroxolamine. Among the oral treatment options, Triazoles include fluconazole and itraconazole. Post-treatment cure rates are 85% within 1-2 weeks. The literature lacks clear data on the effectiveness of treatment for addressing penile or sperm carrier status in asymptomatic sexual partners [12]. Today, it is accepted that oral and vaginal treatments containing fluconazole are inadequate in cases of vaginitis caused by C. glabrata [13]. Therefore, it has been recommended 600 mg of boric acid, Amphotericin B, for 14 days. However, in the presence of resistance, treatment success remains at 17% [15]. In case of treatment failure, fluconazole 800 mg is recommended for 2-3 weeks of treatment, but it is stated that treatment failure is gradually increasing with this treatment method [12]. For this reason, it was put forward that echinocandin and micafungin treatment can be applied in the presence of life-threatening clinical conditions, and it was also stated that this treatment is an unapproved off-label treatment [15].

In our study, patients had previously received oral and topical treatment. Microbiological diagnosis was obtained by detecting causative organisms with cultures. Upon examining the resistance patterns, azole resistance was observed in all cases. The treatment regimen was anidulafungin in four (50%) patients, micafungin in three (37.5%) patients, and caspofungin in a (12.5%) patient. With echinocandin treatment, the clinical and microbiological response was achieved completely, and no early relapse was detected during follow-up. Since the drugs we use are not in the RVVC indication and are used systemically, they are not suitable for use in every patient. However, it can be considered as an alternative treatment in selected cases and in cases where recurrent antifungal use is required due to chronic vaginitis clinic and a cure cannot be achieved. Our study is not sufficient to represent the patient population, and larger, more homogeneous studies are needed. We think that future studies with a larger sample size will provide more definitive guidance.

Limitation

The present study is a limited investigation that demonstrates the efficacy of echinocandin treatment in selected cases based on culture and antifungal susceptibility results. Due to the relatively small sample size, more extensive and controlled studies are needed.

Conclusion

When evaluating treatment options in the RVVC clinic, it is important to consider the patient's previous antifungal regimens, underlying risk factors, and future treatment needs. Azole resistance, particularly in the non-Albicans group, results in non-response to treatment. The infrequent use of vaginal culture in routine practice or the inability of culture results to differentiate between infectious agents and colonization are among the underlying factors for treatment non-response. In selected cases with RVVC clinic, as in our study, echinocandins may be considered as an alternative treatment regimen for cases that are refractory to other treatments or have frequent recurrences.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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